FORM-PTO-1390 (Rev. 9-2001) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER: 025219-366

U.S. APPLICATION NO. (If known, see 37 C.F.R 1.5): Unassigned 09/980788

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/FR00/01556	June 7, 2000	June 8, 1999

TITLE OF INVENTION: CHEMICAL OR BIOLOGICAL ANALYSIS PLATFORM WITH MICRO-BALANCES, DEVICE AND ANALYSIS PROCESS USING THE PLATFORM

APPLICANT(S) FOR DO/EO/US: Philippe PELTIE; Patrice CAILLAT

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☐ This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (21) indicated below.
4. ☒ The US has been elected by the expiration of 19 months from the priority date (Article 31).
5. ☒ A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. ☐ is attached hereto (required only if not communicated by the International Bureau).
   b. ☒ has been communicated by the International Bureau.
   c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☒ An English language translation of the International Application as filed (35 U.S.C. 371(c)(2))
   a. ☒ is attached hereto.
   b. ☐ has been previously submitted under 35 U.S.C. 154(d)(4).
7. ☐ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. ☐ are attached hereto (required only if not communicated by the International Bureau).
   b. ☐ have been communicated by the International Bureau.
   c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
   d. ☐ have not been made and will not be made.
8. ☐ An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. ☒ An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
10. ☐ An English language translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11 to 20 below concern document(s) or information included:

11. ☒ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. ☒ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. ☒ A FIRST preliminary amendment.
14. ☐ A SECOND or SUBSEQUENT preliminary amendment.
15. ☐ A substitute specification.
16. ☐ A change of power of attorney and/or address letter.
17. ☐ A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 35 U.S.C. 1.821 - 1.825.
18. ☐ A second copy of the published international application under 35 U.S.C. 154(d)(4).
19. ☐ A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4).
20. ☒ Other items or information:

PCT Request, Int'l Search Report, Ch. II Demand, Int'l Preliminary Examination Rpt.

21839

U.S. APPLICATION NO. (If known, see 37 C.F.R. 1.5)	INTERNATIONAL APPLICATION NO.	ATTORNEY'S DOCKET NUMBER
Unassigned 09/980788	PCT/FR00/01556	025219-366

21. ☐ The following fees are submitted:	CALCULATIONS	PTO USE ONLY
Basic National Fee (37 CFR 1.492(a)(1)-(5)):		
Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO $1,040.00 (960)		
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO $890.00 (970)		
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO $740.00 (958)		
International preliminary examination fee (37 CFR 1.482) paid to USPTO but all claims did not satisfy provisions of PCT Article 33(1)-(4) $710.00 (956)		
International preliminary examination fee (37 CFR 1.482) paid to USPTO and all claims satisfied provisions of PCT Article 33(1)-(4) $100.00 (962)		
ENTER APPROPRIATE BASIC FEE AMOUNT =	$ 890.00	
Surcharge of **$130.00 (154)** for furnishing the oath or declaration later than 20 ☐ 30 ☐ months from the earliest claimed priority date (37 CFR 1.492(e)).	$	

Claims	Number Filed	Number Extra	Rate		
Total Claims	15 -20 =	0	X$18.00 (966)	$ 0	
Independent Claims	1 -3 =	0	X$84.00 (964)	$ 0	
Multiple dependent claim(s) (if applicable)			+$280.00 (968)	$	

TOTAL OF ABOVE CALCULATIONS =	$ 890.00	
Reduction for 1/2 for filing by small entity, if applicable (see below). +	$	-
SUBTOTAL =	$ 890.00	
Processing fee of **$130.00 (156)** for furnishing the English translation later than 20 ☐ 30 ☐ months from the earliest claimed priority date (37 CFR 1.492(f)). +	$	
TOTAL NATIONAL FEE =	$ 890.00	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). **$40.00 (581)** per property +	$ 40.00	
TOTAL FEES ENCLOSED =	$ 930.00	
	Amount to be refunded:	$
	charged:	$

a. ☐ Small entity status is hereby claimed.

b. ☒ A check in the amount of $ 930.00 to cover the above fees is enclosed.

c. ☐ Please charge my Deposit Account No. 02-4800 in the amount of $_____ to cover the above fees. A duplicate copy of this sheet is enclosed.

d. ☐ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 02-4800. A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

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SIGNATURE

Robert E. Krebs
NAME

25,885
REGISTRATION NUMBER

December 5, 2001
DATE

Patent
Attorney's Docket No. 025219-366

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of	)	
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Peltie, et al.	)	Group Art Unit: Unassigned
	)	
Application No.: Unassigned	)	Examiner: Unassigned
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Filed: Herewith	)	
	)	
For: CHEMICAL OR BIOLOGICAL ANALYSIS PLATFORM WITH MICRO-BALANCES, DEVICE AND ANALYSIS PROCESS USING THE PLATFORM	)	

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Prior to examination, please amend the subject application as follows:

IN THE SPECIFICATION

Please amend the specification by inserting before the first line the sentence:

"This application is a national phase of PCT/FR00/01556 which was filed on June 7, 2000, and was not published in English."

REMARKS

Entry of the foregoing amendment to the Specification is requested to comply with the requirements of 37 C.F.R. 1.78(a)(2).

If the Examiner should be of the opinion that a telephone conference would be helpful in resolving any outstanding issues, the Examiner is urged to contact the undersigned.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

By: _____
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CHEMICAL OR BIOLOGICAL ANALYSIS PLATFORM WITH MICRO-BALANCES, DEVICE AND ANALYSIS PROCESS USING THE PLATFORM

TECHNICAL FIELD

This invention relates to a chemical or biological analysis platform.

This type of platform is usually referred to as detection chips or biochips depending on the application field.

It comprises several sites, for example in the form of micro-dishes. The same or different reagents are placed on each site, that may react selectively with one or several components of a medium to be analysed, called the analyte.

In this presentation, the terms reagent and reaction should be understood in a very broad sense encompassing chemical reactions in the normal sense of the term and also complexing or hybridising phenomena that more specifically concern the biological material, for example such as DNA strands.

The invention also relates to an analysis process and a device for reading analysis platform sites.

Reading may consist of a simple determination for each site, regardless of whether or not a reaction took place. It may also include quantification of the reactions that took place.

The invention is used for applications in the chemical and biological analysis fields, and particularly for DNA sequencing.

STATE OF PRIOR ART

One particular example of an analysis that can be carried out using analysis platforms is sequencing of DNA, as mentioned above.

Analysis platforms, or biochips, comprise a large number of sites on which DNA strands called probes are initially grafted. A different probe is grafted onto each site and forms the "reagent".

When this type of platform is put into contact with a medium to be analysed that also contains DNA strands, hybridising may take place between the strands present in the medium and the probes that are matched with them. Therefore, selective hybridising occurs.

After this operation, the examination of sites determines which sites reacted, in other words sites for which hybridising took place on the probes, so that the composition of the analysed medium, or all or some of the constituents of the analysed medium, can be known.

Different techniques for identifying sites that reacted are known.

A first technique consists of detecting fluorescence of a marker attached to the DNA sample to be analysed.

Another technique consists of detecting electric charges carried by the phosphated skeleton of DNA molecules using a field effect transistor.

These techniques are useful but require preparation of molecules to confer the electrical or emissive property used for their recognition, to them.

Another technique is known in which the DNA probes are fixed onto a quartz plate that is made to vibrate.

When the probe is hybridised, its mass increases and the resonant frequency of the quartz plate reduces. This phenomenon is used to detect hybridising.

However, to achieve a good result, the surface of the quartz plate must be of the order of a few square millimetres. An area of about this magnitude is not compatible with constraints for integration of an ever-increasing number of sites.

The increase in the number of sites on chips is usually accompanied by a reduction in their size, so as to limit the total surface area of the chip.

Yet another technique is known for reading sites without making use of markers. This technique uses an atomic force microscope (AFM) to "map the surface" of the chip. The extreme precision of this type of instrument is sufficient to detect hybridising directly. The principle of the AFM is based on deformation of a micro-structural beam that is brought towards the surface of the chip, the deformation caused by interactions between a point at the end of the structural beam and the scanned area is simply measured by a laser beam reflected by this structural beam.

With a 10 cm lever arm, deformation of the order of one nanometer deflects the laser beam by several microns, which can easily be demonstrated by a network of photo detectors.

However, there are several limitations to atomic force microscopy. Firstly, it is preferably applied in a clean room, and a significant time is necessary to

analyse a site of a biochip. Therefore, it is inconceivable to use an AFM microscope to measure hundreds of sites in parallel. Finally, its cost is far too high to envisage using it at the moment to simply read chips.

A more detailed description of AFM microscopes and associated techniques is given in documents 1, 2, 3, 4, 5, 6, 7, the references of which are given at the end of this description.

DISCLOSURE OF THE INVENTION

The purpose of this invention is to propose an analysis platform and a read device that does not have the limitations mentioned above.

In particular, one purpose is to propose an analysis platform and an analysis method to detect reactions or hybridising that take place without making use of fluorescent markers and without any advance preparation of products to be analysed.

Another purpose is to enable quantification of reactions that took place.

Another purpose is to propose an analysis platform with miniaturized sites that may contain a large number of such sites.

Another purpose of the invention is to propose an analysis method that may be used without requiring a clean room, and that does not disturb the analysed site.

Finally, another purpose of the invention is to propose a simple, reliable and economic platform and a read device.

More precisely, in order to achieve these purposes, the purpose of the invention is a biological or chemical analysis platform comprising a fixed support and at least one first mobile support that may be coated with a reagent, the mobile support being connected to the fixed support by first flexible support means that may be deflected in response to a change in the weight supported by the first mobile support, caused by a reaction of the said reagent.

Each mobile support or at least part of these supports may form an analysis site like that mentioned above, being coated with a chemical or biological reagent. The mobile supports of a particular platform may be coated with different or identical reagents.

The weight supported by the mobile support concerned is modified during a chemical or biological reaction, for example when hybridising a DNA strand with a DNA probe.

In particular, this weight is increased during hybridising.

The weight may also increase or reduce as a result of a modification in the molecular weights of the reagent, when it reacts chemically.

Since the mobile support is held in place by flexible means, in other words means with a certain stiffness, the modification to the weight supported by the mobile support results in a greater or lesser deflection of these means.

The flexible support means comprise at least one flexible structural beam with a first end fixed to the mobile support and the second end fixed to the fixed

support. Note that in a simplified embodiment, the mobile support may be formed by a portion of the flexible structural beam, preferably close to the mobile end of the structural beam.

The beam is a folded beam, for example in spiral form. The fact that the beam is folded into a spiral increases its length and therefore the sensitivity of the device.

More precisely, the invention can be used to measure the displacement amplitude of the mobile support due to the use of support means with a geometry providing high sensitivity defined as the ratio between the weight and the displacement amplitude. As the ratio of the length to the cross-sectional area of the structural beam increases, its sensitivity also increases. Thus, to make a platform with one or several analysis sites on a small area, the invention proposes to use folded beams, for example in the form of a square or circular spiral.

For example, the fixed end of the beam may correspond to the external end of the spiral, while the free central end may support the mobile support.

In an improved embodiment of the platform, the platform may comprise at least one second mobile support associated with the first mobile support, the second mobile support being connected to the said fixed support by second flexible support means, also in the form of a folded beam. The second mobile support is preferably coated with an element of the same mass of the reagent located on the first mobile support, but that does not react with the analyte to be tested. For

example, it may be the same reagent as the reagent that was used to coat the first support, but neutralized. Furthermore, the stiffness of the first and second support means with the associated mobile supports, may advantageously be the same.

Preferably, the first and second mobile supports may be adjacent. The second mobile support is not used as an analysis site, but is used as a reference to make differential measurements. These measurements are then less affected by measurement conditions and give better sensitivity.

Although it is not essential, the use of double mobile supports is particularly appropriate when it is required to quantify a reaction that took place, by measuring the difference in the weight of the reagent.

For example, this is useful for determining the length and/or number of hybridised DNA strands.

In a simpler analysis, such as an On/Off type analysis, it may be preferable to use a simpler device with a lower measurement precision.

In one particular embodiment, the platform may comprise a first flexible structural beam to support the first mobile support, and a second flexible beam to support the second mobile support, the first and second beams having adjacent parallel segments.

Due to the adjacent parallel segments, the flexible beams in each pair of mobile supports are subjected to approximately the same outside measurement conditions and a large gain in the size can be obtained.

As will become clearer in the rest of the description, the deflection, in other words the displacement of mobile supports, may be measured by the reflection of a laser beam.

This can be done by providing the mobile support or a part fixed to the mobile support with a surface that will reflect a laser beam.

The invention is also applicable to a device for reading an analysis platform like that described. The device comprises a light source capable of producing a reading light beam, means of transferring the beam to at least one mobile support, and means of receiving a beam reflected away from the mobile support and detecting displacements of the said reflected beam.

The means of reception of the reflected beam and the means of detecting its displacements may comprise several photo detectors. When the photo detectors are scanned by the reflected beam, the displacement amplitude of the beam is determined, for example as a function of the number of scanned photo detectors.

Since the displacement amplitude of the beam is related to the displacement of the mobile support or to the deflection of the flexible means of holding the mobile support, this value can be calculated.

The value corresponding to the displacement of the mobile support is an output value from the device that can be displayed or recorded for subsequent data processing.

The device may also comprise means of relative displacement of the read beam and the platform to scan several mobile supports on the platform with the beam.

These means can be used to explore several sites in sequence, in other words several mobile supports. For example, they comprise a rotating plate or a translation table to move the analysis platform in front of a read light source.

The read light source and the means of reception of the reflected beam may also be designed to move.

Finally, several read light sources associated with several reflected beam reception means may be provided to read several sites at the same time.

The invention also relates to a biological or chemical analysis process using an analysis platform and possibly a read device like that described.

According to this process:

- at least one mobile support is coated with a reagent, the weight of which may be modified during a chemical or biological reaction,

- the support is put into contact with a medium to be analysed that may contain compounds that could react with the said reagent to modify its weight,

- any displacement of the mobile support is detected by means of a light beam directed towards and reflected away from the mobile support.

The mobile support displacement may be detected either by a simple On/Off type detection, in other words a detection to determine whether or not the mobile support moved.

The purpose of detection may also be to measure the displacement amplitude of the mobile support, so that the change in weight of the mobile structure can

be calculated, knowing the stiffness of the flexible support means in the mobile support.

Detection, in other words the measurement of the displacement amplitude of the mobile support, may be an absolute measurement or a relative measurement relative to a second mobile support that is almost identical except that it is neutral, as mentioned above.

Finally, another purpose of the invention is a process for making an analysis platform like that described. According to this process:

- an etching mask is formed on a substrate with a sacrificial layer placed between a thin surface layer and a base layer, the etching mask having a pattern that defines the location and dimensions of the mobile support and the flexible support means,

- the thin surface layer is formed by etching, using the mask pattern,

- the sacrificial layer is selectively eliminated to release the mobile support and the associated support means.

The etching applied firstly to form the thin surface layer and secondly for local elimination of this sacrificial layer are preferably selective etchings that attack the material in the thin surface layer or in the buried surface layer in preference.

For example, the substrate used is a silicon on insulator (SOI) type substrate in which the base layer and the thin surface layer are made of silicon and in which the buried layer is made of silicon oxide.

Other characteristics and advantages of this invention will become clearer from the following

description made with reference to the figures in the attached drawings.

This description is given purely for illustrative purposes and is non-limitative.

BRIEF DESCRIPTION OF THE FIGURES

- Figure 1 shows a diagrammatic and simplified representation of part of an analysis platform and a read device according to the invention.

- Figure 2 shows another simplified scheme illustrating the principle used to read the platform.

- Figure 3 is a graph showing a deflection amplitude of mobile supports of the different platforms as a function of a change in the weight supported by the mobile supports of these platforms.

- Figures 4 to 8 are diagrammatic sections of a substrate illustrating the successive steps of manufacturing an analysis platform according to the invention.

DETAILED DESCRIPTION OF EMBODIMENTS OF THE INVENTION

The following description is specifically applicable to a particular analysis site of a platform. However, note that the same platform may include many such sites.

For example, the same platform may comprise up to 1000 analysis sites.

In figure 1, reference 102 shows a particular site of a platform 100 equipped with several sites.

Each site comprises two associated mobile supports 104a, 104b.

The first mobile support 104a is equipped with one or several DNA strands 106a grafted onto its surface and that can be selectively hybridised with matched strands placed in a solution or a medium to be analysed.

The second mobile support 104b is associated with the first support, and is located close to it and is equipped with identical but neutralized, in other words non hybridised, DNA strands 106b, or a molecule with the same weight. It may also have no reagent. Although they are close together, the two mobile supports are independent of each other. The second mobile support is used as a "reference" since it carries a neutralized probe. Reading after hybridising is a differential read between the deflection of the beam 108a supporting the first mobile support and deflection of a beam 108b supporting the second mobile support.

Each mobile support is connected to a fixed support 110 through a flexible beam 108a, 108b respectively. The fixed support 110 may for example be a rigid platform frame extending between the sites, or at the periphery of the sites 100.

The figure shows that the mobile supports 104a, 104b are formed simply by the free ends of the flexible beams 108a, 108b. Consequently, the free ends of the beams are widened.

The flexible beams are folded according to a square spiral pattern. They have one fixed end fixed to the fixed support 110 and a mobile end fixed to the

mobile support associated with or directly forming the mobile support.

On the example in the figure, the flexible beams 108a, 108b on each site extend concentrically to make up parallel and adjacent straight line segments.

The length of the longest external segments may be of the order of 100 to 150 µm, which is approximately the dimension of the side of one site 102.

The beams that are only held by their fixed end may deflect in response to a change in the weight supported by the corresponding mobile supports.

Therefore the deflection and consequently the displacement of the supports takes place in preference along a Z direction shown in the figure that is perpendicular to the main plane of the platform.

The maximum measurement sensitivity is obtained when the Z direction is approximately parallel to the earth's gravitation field, which is the natural situation if the platform is placed on a horizontal work plane.

The deflection amplitude in response to a given weight change depends on many parameters. Among these are the length and shape of the beams 108a, 108b, and their thickness, width and material used. These parameters may be adjusted to obtain a required stiffness constant.

Examples of possible choices for parameters are indicated in the rest of the description with relation to figure 4.

Note that several forms of flexible beams may be envisaged. Furthermore, other embodiments of flexible support means for the mobile support may be envisaged.

Reference 120 denotes a read light source. For example, it may be a laser emitting one or several parallel beams 122.

The laser beam is directed to the mobile supports from which it is reflected. The reflection may take place on mobile supports, at one end of the flexible beams or possibly on reflecting surfaces fixed to the mobile supports.

The reflected beam(s) 124a, 124b are directed towards a set of photoelectric detectors 126 capable of detecting a displacement of beams and possibly measuring the amplitude of the displacements.

The photo detectors are connected to recording and operating means, for example in the form of a computer 128.

In the example shown in the figure, two beams 124a and 124b are reflected away from two mobile supports 104a and 104b.

The reception of the two beams on the photoelectric detectors can be used either to make independent measurements or to make a differential measurement.

In the example shown, the platform 100 is placed on a translation table 103 that moves the platform 100 along either of the X or Y directions perpendicular to the Z direction already mentioned.

The platform is displaced so as to scan several sites with the same light source for successive measurements.

The light source 120 and the photoelectric detectors 126 may also be designed so that they can be moved if necessary.

Figure 2 diagrammatically shows how the deflection of the flexible support means results in a displacement of the reflected beam.

In figure 2, identical elements and elements similar to those in figure 1 have the same references plus 100.

Figure 2 shows a mobile support 204 held in place by a flexible beam 208 with length L, the length L being measured from a fixed point to the centre of gravity of the mobile support. (The beam in figure 2 is a straight beam, for simplification reasons). The support is shown as a solid line in its rest position and in a position in which the beam is deflected. This second position called the "deflected position" is shown as a discontinuous line.

In the rest position of the mobile support 204, a laser beam 222 originating from a source 220 is reflected forming a reflected ray 224r.

The reflected ray 224r, in the rest position, is incident to a set of detectors 226 at a first position 227r.

In the deflected position of the mobile support 204, a reflected ray 224d is incident to the detectors in a second position 227d offset from the first.

For a given beam length L, a deflection angle α results in a displacement D of the reflected beam between the first and second positions 227r, 227d on the detectors 226.

The figure also shows the deflection d between the two positions of the mobile support 2°4.

In the example in the figure for a beam 240 with a length of 100 nm, with a mobile support for which the half-length *l* is 40 µm, a deflection d equal to 1 nm results in a 2.5 µm displacement D of the beam on the detectors.

Figure 3 is a logarithmic graph that shows the deflection of a beam at its end as the ordinate, as a function of the variation in weight supported by the mobile support.

The deflection corresponding to the deflection d in figure 2 is indicated as the ordinate and is expressed in nanometers.

The variation in the weight (mass) is shown as the abscissa and is expressed in nanograms.

Curves C_1, C_2 and C_3 on the graph are produced with a device according to figure 1, in which the longest external straight line segment of the spiral folded beam is 150 µm, and in which the segments are at a spacing of 5 µm.

For curve C_1, the width of the beam is 5 µm and its thickness is 1 µm.

For curve C_2, the width of the beam is 5 µm and its thickness is 3 µm.

For curve C_3, the width of the beam is 5 µm and its thickness is 5 µm.

A linearity can be seen between the variation of the weight and the deflection. The straight line curves C_1, C_2, C_3 have a slope that characterizes the stiffness of the flexible support means (beam). The variation of the weight as a function of the amplitude of the recorded deflection is determined, knowing the stiffness curve (straight line) of the graph.

The stiffness of the flexible means is preferably adjusted such that most of the part of the characteristic curve corresponding to the envisaged weight variation range is located above a line denoted I. Line I corresponds to deflections for which the amplitude is equal to or greater than 1 nm. These deflections are more easily detectable.

Figures 4 to 8 described below indicate the steps in a process for manufacturing a platform according to the invention.

For simplification reasons, only part of a platform consisting of a single analysis site is shown.

Figure 4 shows an initial substrate 10 comprising a thick base layer 12 acting as a support, an intermediate sacrificial layer 14 and a thin surface layer 16.

For example, the substrate may be an SOI (Silicon On Insulator) type substrate in which the base layer and the surface layer are made of silicon and in which the intermediate layer is made of silicon oxide.

The surface layer 16 is used to make a flexible beam that is terminated by a mobile support like that described previously.

The thickness of the thin surface layer 16 can be modified, to adjust the stiffness of the beam.

Consequently, the thickness of the surface layer 16 can be precisely adjusted by silicon epitaxy.

Figure 5 shows the formation of a mask 18 on the surface layer 16. The mask has a pattern corresponding to the shape and location of the flexible beam and the mobile supports to be made.

The mask itself is shaped by insolation and is developed using the usual micro-electronic techniques.

A first selective etching of silicon then takes place to eliminate the part of the thin silicon layer not protected by the mask. The structure obtained in figure 6 is thus obtained.

For example the first etching is of the dry type using "Reactive Ion Etching", for example in SF_6 or BCl_3.

This etching is selective with respect to silicon oxide such that it is stopped by the buried sacrificial layer 14. Consequently the base layer 12 is protected.

Figure 7 shows the structure obtained after eliminating mask 18. This figure shows two segments 20 of the flexible beam seen in section and part of the fixed support 22.

A second selective chemical (FH) etching of the sacrificial silicon oxide layer can eliminate this layer under the mobile parts, in other words in particular under the segments 20 of the flexible beam.

Figure 8 shows that the second etching also eliminates part of the sacrificial layer corresponding to the fixed support, in other words particularly at

the fixed end of the beam. However in these regions, the sacrificial layer is not completely eliminated such that the fixed support 22 and in particular the fixed end of the beam remain firmly fixed to the base layer 12.

DOCUMENTS MENTIONED

(1)

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(2)

"Analysis and design of an interdigital cantilever as a displacement sensor"
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(3)

"Independent detection of vertical and lateral forces with a sidewall-implanted dual-axis piezoresistive cantilever"
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(4)

"Microfabrication of new sensors for scanning probe microscopy"
W. Noël, - Journ. Micromech., 8, 1998.

(5)

"High resolution analysis of biological samples by scanning probe microscopy"
W.B. Stine, Europ. Micro. and Anal., November 1995.

(6)

"Microstructured polymer tips for scanning near field optical microscopy"
H. Stürmer, Ultramicroscopy 71, 1998.

(7)

"Balance approach for mechanical properties test of micro fabricated structure"
X. Xiong, SPIE, Vol. 3223.

CLAIMS

1. Biological or chemical analysis platform (10, 102) comprising at least one fixed support (12, 22, 110) and at least one first mobile support (104a, 204) that may be coated with reagent, the mobile support being connected to the fixed support by first flexible support means (20, 108a, 208) that may be deflected in response to a change in weight supported by the first mobile support, the flexible support means comprising at least one folded flexible beam with at least one end fixed to the mobile support and a second end fixed to the fixed support.

2. Platform according to claim 1, in which the first mobile support (104a) is coated with a chemical reagent or a biological reagent.

3. Platform according to claim 2, comprising at least one second mobile support (104b) associated with the first mobile support (104a), the second mobile support being connected to the said fixed support (110) by second flexible support means (108b) and being coated with a non-reactive material so as to have a mass equal to the mass of the first support coated with reagent.

4. Platform according to claim 1, in which part of the structural beam close to its first end forms the mobile support.

5. Platform according to claim 3, comprising a first flexible support beam (108a) for the first mobile support (104a) and a second flexible support beam (108b) for the second mobile support (104b), the first and second beams having adjacent parallel segments.

6. Platform according to claim 5, in which the first and second supports are approximately identical and in which the first and second beams have approximately the same stiffness coefficients.

7. Platform according to claim 1, in which the beam has a spiral shape and the mobile support is formed approximately at the centre of the spiral.

8. Platform according to claim 1, in which the mobile support or at least a fixed part to the mobile support has a reflecting surface for a laser beam.

9. Platform according to claim 1, comprising several mobile supports connected to the fixed support.

10. Device for reading a platform according to claim 1, comprising at least one light source (120, 220) capable of producing a read light beam, means (126, 226) of directing the beam towards at least one mobile support, and means of reception of a reflected beam from the mobile support, and detection of displacements of the said reflected beam.

11. Device according to claim 10, in which the means (126, 226) of reception of the reflected beam and the means of detecting displacements are provided with several photodetectors.

12. Device according to claim 10, in which means of directing the beam towards at least one mobile support comprise means (103) for relatively displacing the beam and the platform to scan several mobile supports on the platform with the beam.

13. Biological or chemical analysis process using one platform conform with claim 1, in which:

- at least one mobile support is coated with a reagent, the weight of which may be modified as a result of a chemical or biological reaction,

- the support is put into contact with a medium to be analysed that could contain compounds that could react with the said reagent in order to modify its weight,

- any displacement of the mobile support is detected by means of a light beam directed towards and reflected away from the mobile support.

14. Process for manufacturing an analysis platform according to claim 1, in which:

- an etching mask (18) is formed on a substrate (10) with a sacrificial layer (14) arranged between a thin surface layer (16) and a base layer (12), the etching mask having a pattern that defines the location

and dimensions of the mobile support and the flexible support means,

- the thin surface layer is shaped by etching according to the pattern of the mask,

- the sacrificial layer is selectively eliminated to release the mobile support and the associated support means.

15. Process according to claim 14, in which the substrate is of the silicon on insulator (SOI) type in which the base layer and the thin surface layer are made of silicon and in which the buried layer is made of silicon oxide.

FIG. 1

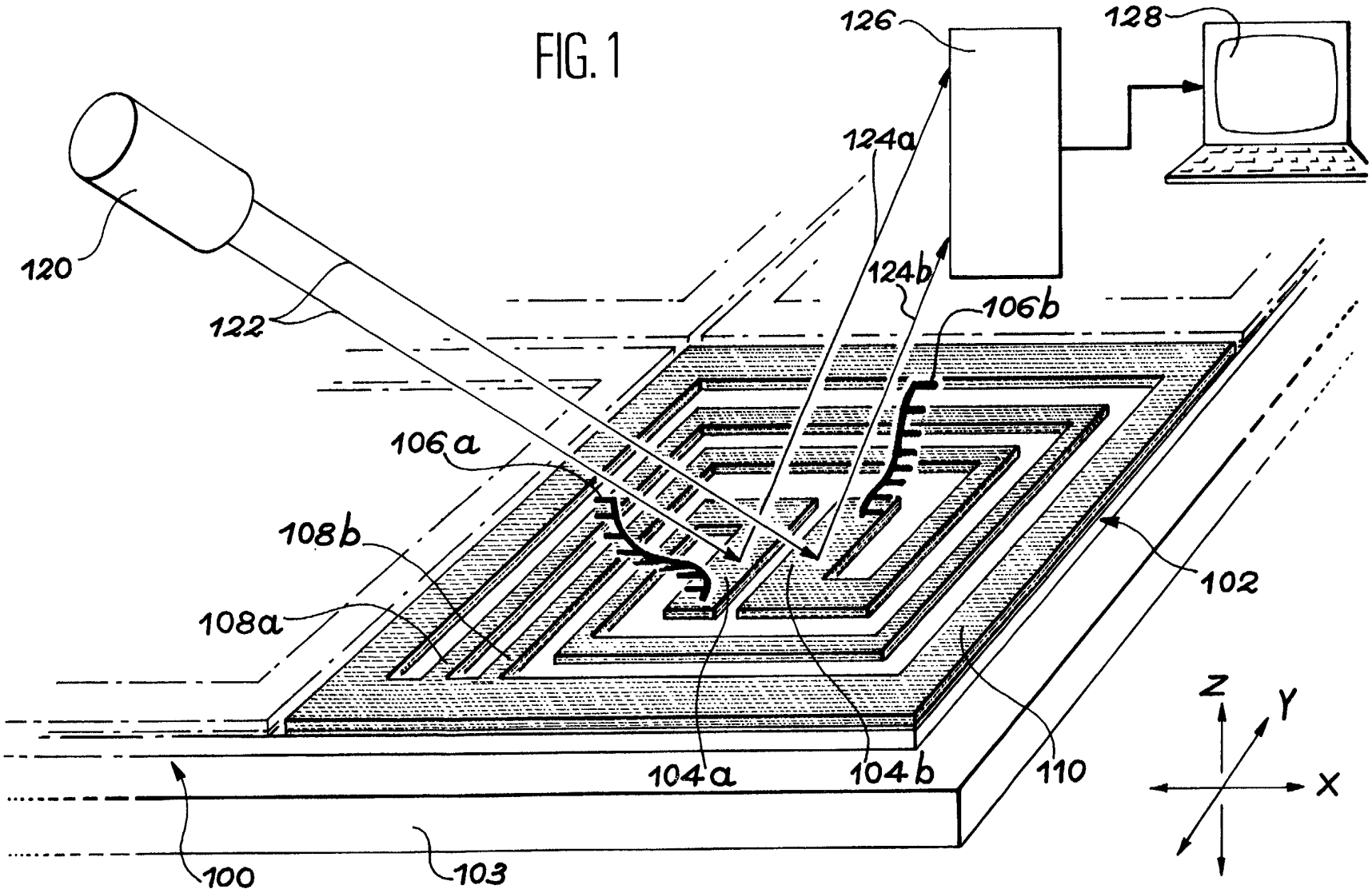
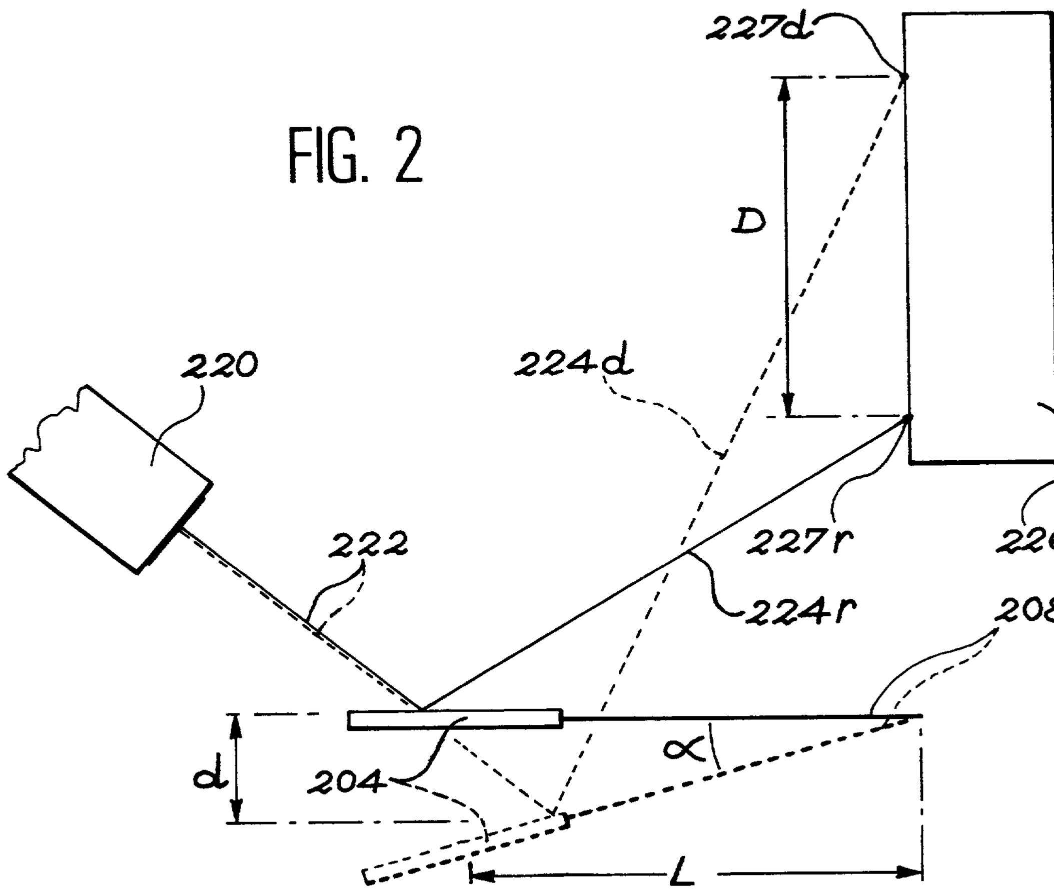


FIG. 2



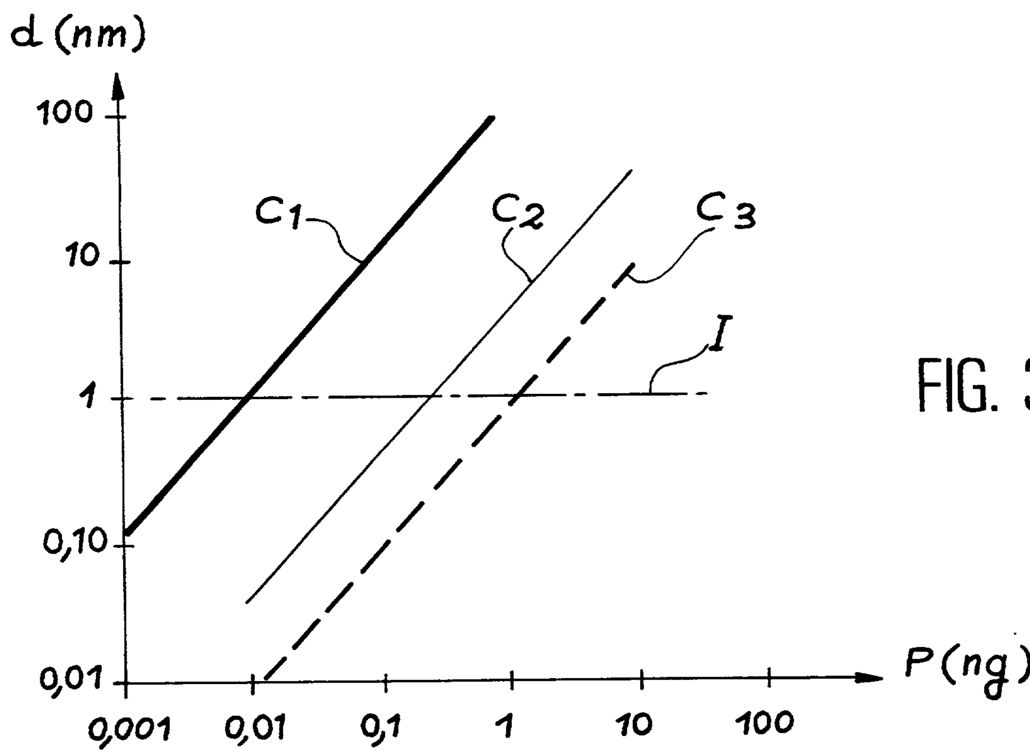


FIG. 3

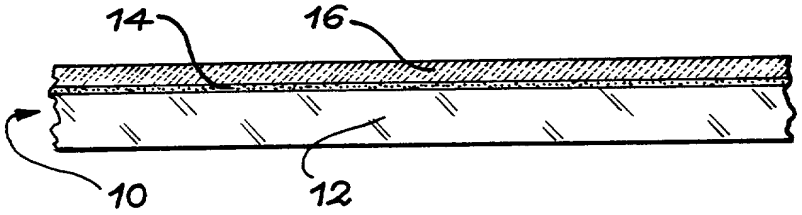


FIG. 4

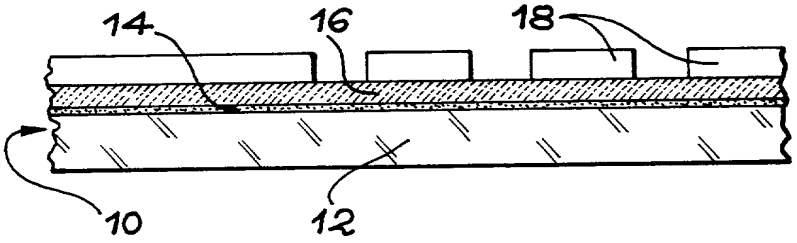


FIG. 5

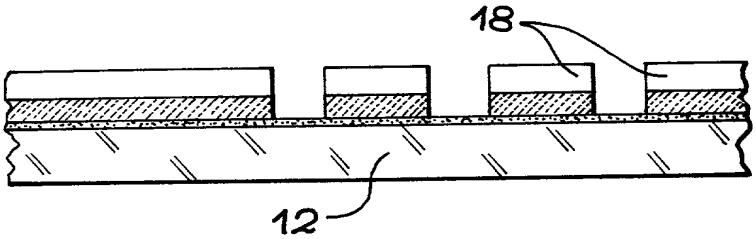


FIG. 6

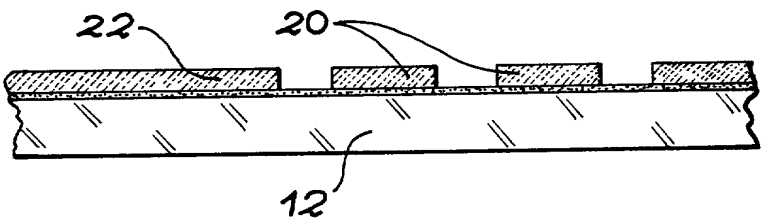


FIG. 7

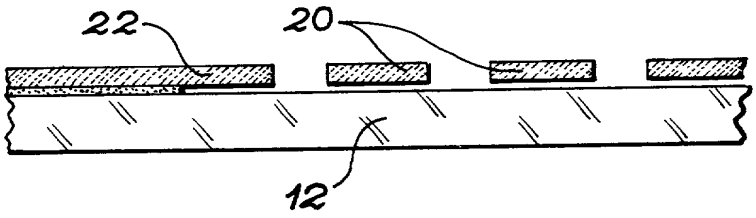


FIG. 8

B 13265.3 EW

Declaration, Power Of Attorney and Petition

WE (I) the undersigned inventor(s), hereby declare(s) that :

My residence, post office address and citizenship are as stated below next to my name,

We (I) believe that we are (I am) the original, first, and joint (sole) inventor(s) of the subject matter which is claimed and for which a patent is sought on the invention entitled

CHEMICAL OR BIOLOGICAL ANALYSIS PLATFORM WITH MICRO-BALANCES, DEVICE AND ANALYSIS PROCESS USING THE PLATFORM

the specification of which

- ☐ is attached hereto.
- ☐ was filed on
  as Application Serial No.
  and amended on
- ☒ was filed as PCT international application
  Number PCT/FR00/01556
  on June 07, 2000
  and was amended under PCT Article 19
  on

We (I) hereby state that we (I) have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

We (I) acknowledge the duty to disclose information known to be material to the patentability of this application as defined in Section 1.56 of Title 37 Code of Federal Regulations.

We (I) hereby claim foreign priority benefits under 35 U.S.C. § 119 (a)-(d) or § 365 (b) of any foreign application(s) for patent or inventor's certificate, or § 365 (a) of any PCT International application which designated at least one country other than the United States, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate, or PCT International application having a filing date before that of the application on which priority is claimed. Prior Foreign Application (s)

Application No.	Country	Day/month/Year	Priority Claimed
99 07201	FRANCE	08 JUNE 1999	☒ YES ☐ NO
			☐ YES ☐ NO
			☐ YES ☐ NO
			☐ YES ☐ NO

We (I) hereby claim the benefit under Title 35, United States Code, § 119 (e) of any United States provisional application(s) listed below.

(Application Number) (Filing Date)

(Application Number) (Filing Date)

We (I) hereby claim the benefit under 35 U.S.C. §120 of any United States application(s), or § 365(c) of any PCT International application designating the United States, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of 35 U.S.C. § 112, I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR § 1.56 which became available between the filing date of prior application and the national or PCT International filing date of this application.

Application Serial No.	Filing Date	Status (pending, patented, abandoned)

And we (I) hereby appoint :William L. Mathis, Registration Number 17,337; Alan E. Kopecki, Registration Number 25,813; Eric H. Weisblatt, Registration Number 30,505; Peter H. Smolka, Registration Number 15,913; Regis E. Slutter, Registration Number 26,999; James W. Peterson, Registration Number 26,057; Robert S.Swecker, Registration Number 19,885, Samuel C. Miller III, Registration Number 27,360; Terase Stanek REA, Registration Number 30,427; Platon N. Mandros, Registration Number 22,124; Ralph L. Freeland Jr., Registration Number 16,110; Robert E. Krebs, Registration Number 25,885; Benton S. Duffett jr., Registration Number 22,030; Robert M. Schulman, Registration Number 31,196; Joel M. Freed, Registration Number 25,101; James A. Labarre, Registration Number 28,632; William C. Rowland, Registration Number 30,888; Norman H. Stepno, Registration Number 22,716; E. Joseph Gess, Registration Number 28,510; Richard H. Kjeldgaard, Registration Number 30,186; Ronald L. Grudziecki, Registration Number 24,970; David D. Reynolds, Registration Number 29,273; T. Gene Dillahunty, Registration Number 25,423; Frederick G. Michaud Jr, Registration Number 26,003; R. Danny Huntington, Registration Number 27,903 and Anthony W. Shaw, Registration Number 30,104; our (my) attorneys, with full powers of substitution and revocation, to prosecute this application and to transact all business in the Patent Office connected therewith; and we (I) hereby request that all correspondence regarding this application be sent to the firm of BURNS, DOANE, SWECKER & MATHIS, whose post Office Address is : George Mason Building, Washington and Prince Streets, P.O. Box 1404 Alexandria, Virginia 22313-1404.

We (I) declare that all statements made herein of our (my) own knowledge are true and that all statements made on information and belief are believed to be true ; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such wilful false statements may jeopardise the validity of the application or any patent issuing thereon.

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Date

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Signature of Inventor

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